

Fig. 1 is a schematic cross-sectional view of a multi-layered, elongated device. The device has an outer shell (10) with a top flange (9) and a bottom flange (8). The shell is composed of multiple layers (11, 12, 13, 14, 15). The interior contains a central region (19) with numerous small dots (12) and a bottom region (18) with vertical lines. A central opening (13) is visible at the top.

FIG. 4

A bar chart illustrating the release rate of 100 mg of 1% w/v hydrocortisone acetate over a 14-hour period. The y-axis represents the release rate in mg/hr, ranging from 0.00 to 50.00. The x-axis represents time in hours, ranging from 0.00 to 14.00. The release rate starts at approximately 20 mg/hr at 0 hours and decreases steadily to about 5 mg/hr at 14 hours. Error bars are included for each measurement.

Time (Hours)	Release Rate (mg/hr)
0.00	20.00
1.00	25.00
2.00	26.00
3.00	24.00
4.00	23.00
5.00	22.00
6.00	21.00
7.00	20.00
8.00	19.00
9.00	18.00
10.00	16.00
11.00	12.00
12.00	10.00
13.00	8.00
14.00	5.00

Figure 1 is a line graph showing the cumulative amount of dose (%) versus time (hours) for the release of 100 mg of 10% w/v polyvinyl alcohol solution from a 10% w/v polyvinyl alcohol solution. The y-axis is labeled 'CUMULATIVE AMOUNT OF DOSE (%)' and ranges from 0.00 to 100.00. The x-axis is labeled 'TIME (HOURS)' and ranges from 0.00 to 14.00. The graph shows a linear increase in cumulative dose over time, reaching approximately 95% at 14 hours. Error bars are included for each data point.

Time (Hours)	Cumulative Amount of Dose (%)
0.00	0.00
0.50	2.00
1.00	4.00
1.50	6.00
2.00	8.00
2.50	10.00
3.00	12.00
3.50	14.00
4.00	16.00
4.50	18.00
5.00	20.00
5.50	22.00
6.00	24.00
6.50	26.00
7.00	28.00
7.50	30.00
8.00	32.00
8.50	34.00
9.00	36.00
9.50	38.00
10.00	40.00
10.50	42.00
11.00	44.00
11.50	46.00
12.00	48.00
12.50	50.00
13.00	52.00
13.50	54.00
14.00	56.00

FIG. 5B

A ternary phase diagram for the EL/Myvacet/Water system. The vertices represent 100% of each component: Water (top), EL (bottom-left), and Myvacet (bottom-right). The diagram is divided into regions by a boundary line. The region above the line is labeled 'EL/Myvacet 25/75' and contains inverted triangles. The region below the line is labeled 'Microemulsion' and contains circles. The boundary line is labeled with ratios: 50/50, 75/25, and 100/0. The axes are marked with percentages from 0 to 100.

Cremophor EL
FIG. 7

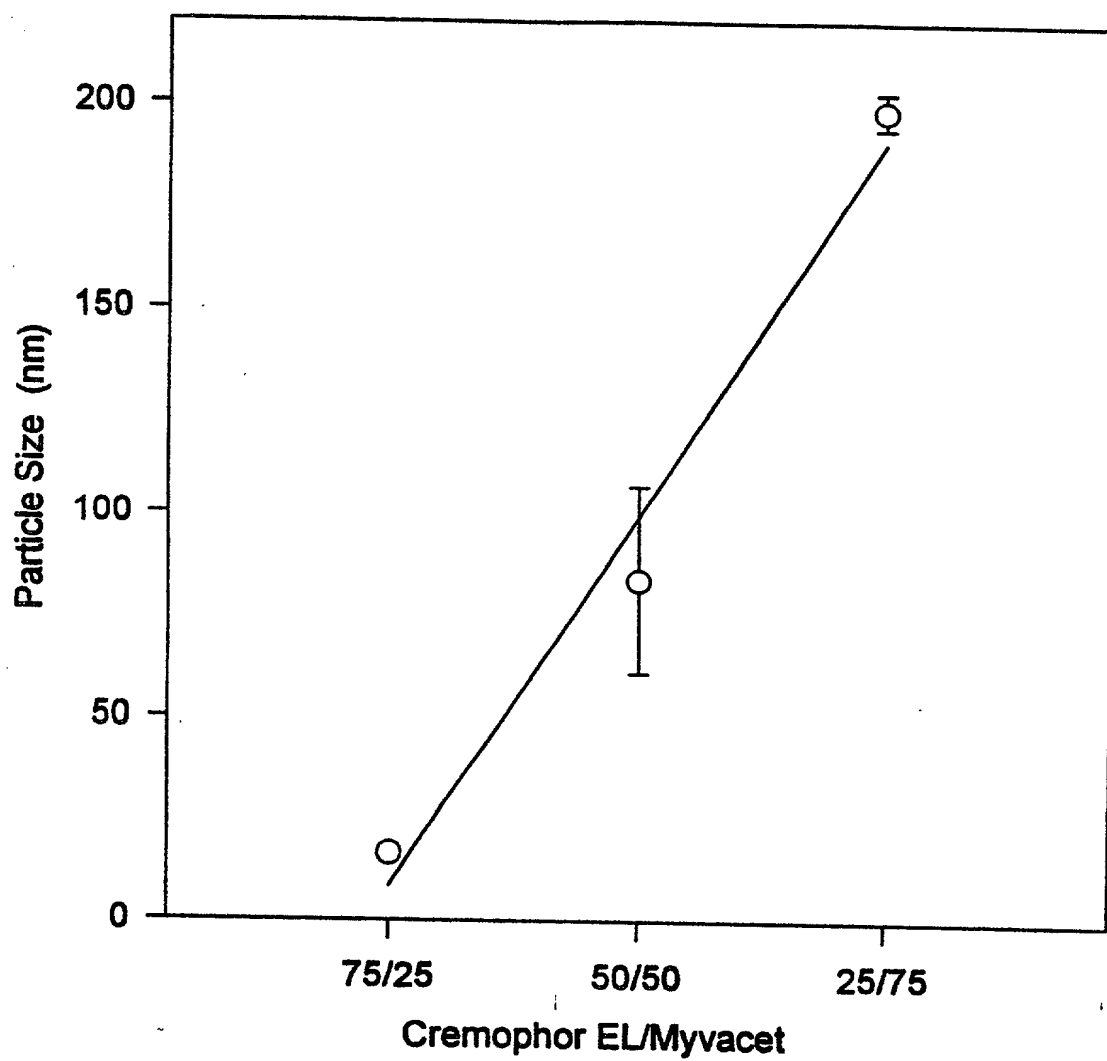


FIG. 8

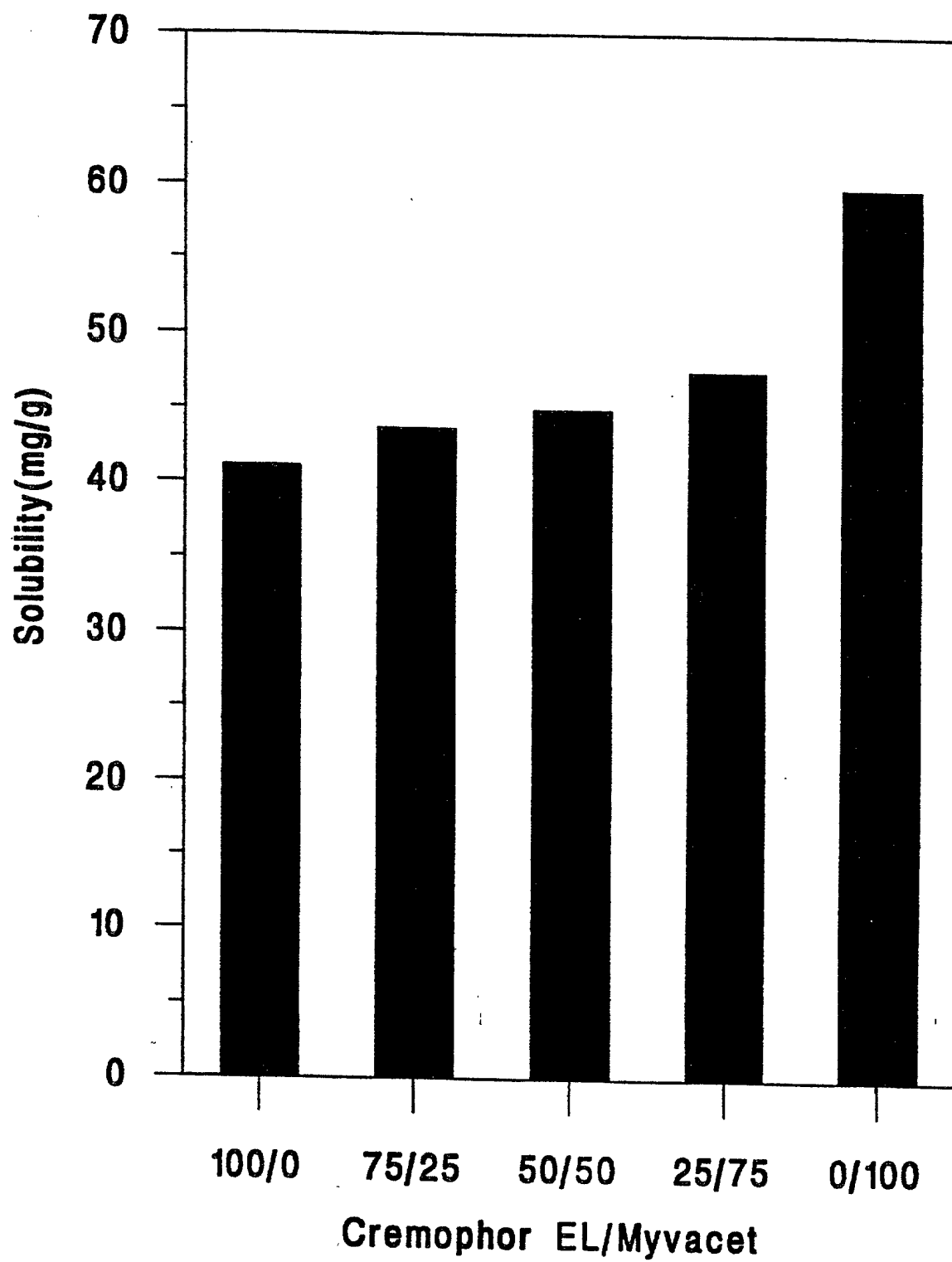


FIG. 9

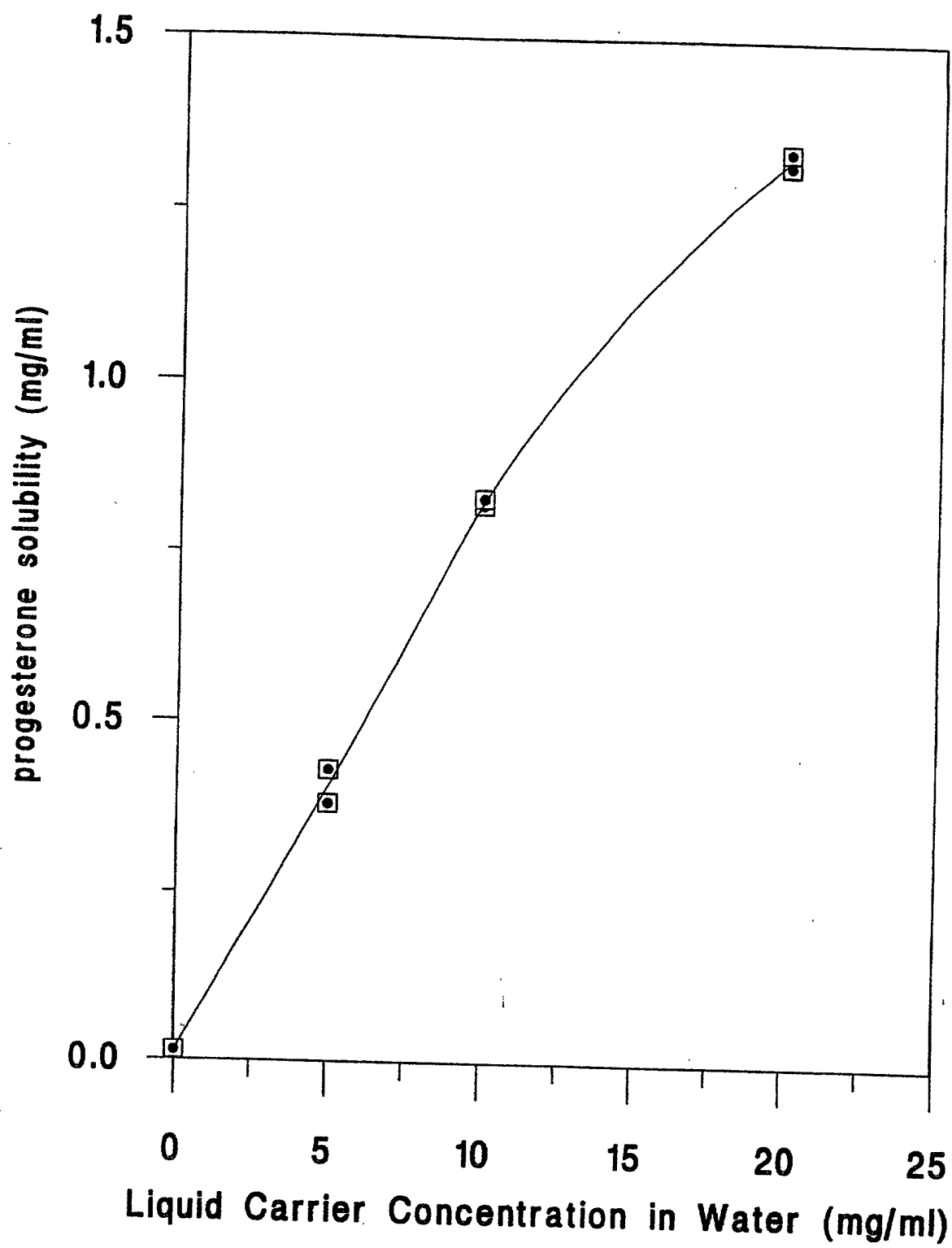
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FIG. 10

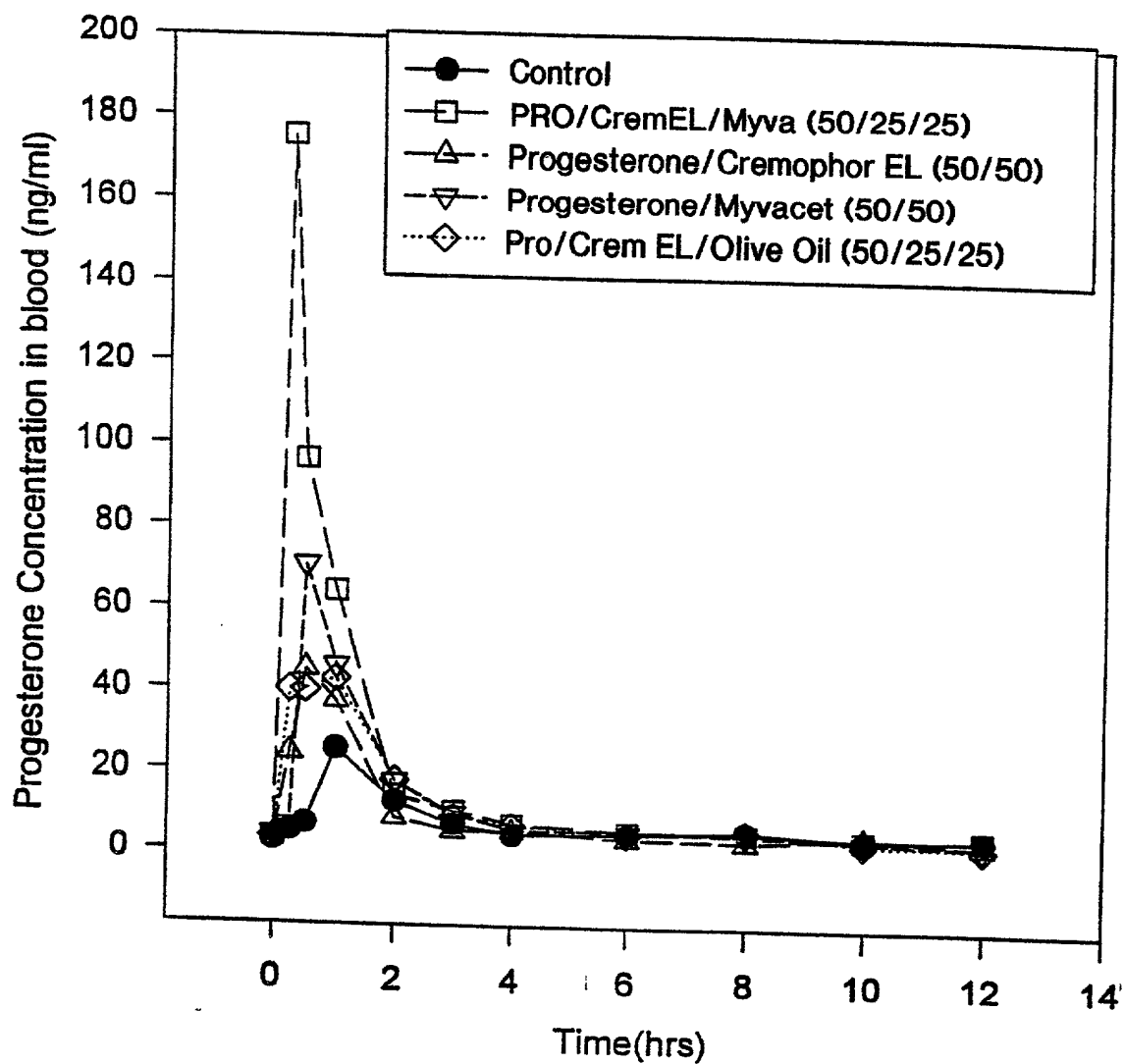


FIG. II

Progesterone Concentration in Blood Serum (ng/ml)

Time (hrs)

Legend:

- in dog 1 (solid line, filled circle)
- in dog 2 (solid line, filled square)
- in dog 3 (solid line, filled triangle)
- in dog 1 (dashed line, open circle)
- in dog 2 (dashed line, open square)
- in dog 3 (dashed line, open triangle)

Time (hrs)	in dog 1 (solid)	in dog 2 (solid)	in dog 3 (solid)	in dog 1 (dashed)	in dog 2 (dashed)	in dog 3 (dashed)
0	~5	~5	~5	~5	~5	~5
1	~10	~10	~10	~250	~90	~160
2	~10	~10	~10	~10	~10	~10
3	~5	~5	~5	~5	~5	~5
4	~5	~5	~5	~5	~5	~5
6	~5	~5	~5	~5	~5	~5
8	~5	~5	~5	~5	~5	~5
10	~5	~5	~5	~5	~5	~5
12	~5	~5	~5	~5	~5	~5

FIG. 12

Time (hrs)	in dog 1 (0h)	in dog 2 (0h)	in dog 3 (0h)	in dog 1 (2h)	in dog 2 (2h)	in dog 3 (2h)	in dog 1 (4h)	in dog 2 (4h)	in dog 3 (4h)
0	0	0	0	0	0	0	0	0	0
1	1800	1200	1200	1800	1200	1200	1800	1200	1200
2	4700	3300	5100	4700	3300	5100	4700	3300	5100
3	700	400	1300	700	400	1300	700	400	1300
4	1500	1000	1000	1500	1000	1000	1500	1000	1000
6	500	200	200	500	200	200	500	200	200
8	200	100	100	200	100	100	200	100	100
10	100	50	50	100	50	50	100	50	50
12	50	20	20	50	20	20	50	20	20

FIG. 13

**Pharmacokinetic Data for Oral Progesterone
Formulations Dosed to Dogs (40mg)**

Formulation #	T _{max} (h)				C _{max} (ng/ml)				AUC (ng/ml*h)		*Relative BA % Average (s.d)	
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).				
1	1	1	1	1	38.4	13.9	24.4	25.6(12.3)	104	51	104	100
2	0.25	0.50	0.25	0.33	252	90.8	248	197(92)	226	113	265	232 (21)
3	0.50	0.25	0.50	0.42	53.4	57.7	33.7	48.3(12.8)	109	95	102	130 (50)
4	0.5	1	1	0.83	174	57.1	30.4	87.2(76.4)	167	289	73	176(108)
5	0.5	1	0.25	0.58	57.2	70.8	74.7	67.5(9.1)	114	342	86	181(141)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).

The relative bioavailability is the ratio of AUC for liquid formulations to that for laqueus drug-layer formulation.

Formulation Composition (wt%)

Components	Formulation #				
	1	2	3	4	5
Progesterone	60	4	4	4	4
Mannitol	21				
Ac-di-sol	10				
Myji 52-s	5				
HPMC E-5	3				
Mg stearate	1				
Cremophor EL		48	96		48
Myvacet 9-45		48			
Olive oil				96	48

FIG. 14

**Pharmacokinetic Data for Emulsion Progesterone Formulation and
Nonemulsion Push-Pill Drug-Layer Formulation (300mg dose)**

Formulation #	T _{max} (h)				C _{max} (ng/ml)			AUC (ng/ml*h)				Relative BA (%) Average (s.d)	
	Dog 1	2	3	Avg	Dog 1	2	3	Dog 1	2	3	Avg.(s.d)		
Nonemulsion	2	1	1	1.33	489	778	649	639(145)	1101	1715	898	1238(425)	100
Emulsion	1	1	1	1	4800	3420	5180	4467(926)	7715	4708	7418	6614(1657)	600 (289)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).
The relative bioavailability is the ratio of AUC for liquid formulations to that for MPA-22 drug-layer formulation.

Formulation Composition (wt%)

Components	Nonemulsion Drug-Layer	Emulsion Oral Formulation
Progesterone	60	50
Mannitol	21	
Ac-di-sol	10	
Myji 52-s	5	12.5
HPMC E-5	3	
Mg stearate	1	
Cremophor EL		25.0
Myvacet 9-45		12.5

FIG. 15